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      (FILE 'HOME' ENTERED AT 14:51:34 ON 03 OCT 2003)

      FILE 'USPATFULL' ENTERED AT 14:51:44 ON 03 OCT 2003
L1              0 S 6495601/PN
L2              1 S US6495601/PN
                E COTRANSPORTER ANTAGONIST/CT

      FILE 'MEDLINE' ENTERED AT 14:53:26 ON 03 OCT 2003
                E COTRANSPORTER ANTAGONIST/CT
                E E6+ALL

      FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, USPATFULL, JAPIO' ENTERED AT
      14:54:38 ON 03 OCT 2003
L3           2778 S SODIUM-POTASSIUM-CHLORIDE SYMPORTERS OR SODIUM-POTASSIUM-CHLO
L4         133279 S FUROSEMIDE OR DIURETICS OR THIAZIDE OR HYDROCHLOROTHIAZIDE
L5         763515 S MIGRAINE OR HEADACHE OR DEPRESSION
L6             30 S L3 AND L5
L7           5340 S L4 AND L5
L8             26 DUP REM L6 (4 DUPLICATES REMOVED)
L9             26 FOCUS L8 1-

      FILE 'REGISTRY' ENTERED AT 15:00:43 ON 03 OCT 2003
L10            20 S FUROSEMIDE

      FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, USPATFULL, JAPIO' ENTERED AT
      15:01:38 ON 03 OCT 2003
L11             0 S L7 AND 5431-9/RN
L12           110 S L7 AND 54-31-9/RN
L13           106 DUP REM L12 (4 DUPLICATES REMOVED)
L14           106 FOCUS L13 1-

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CCESSION NUMBER: 1991:240451 CAPLUS
DOCUMENT NUMBER: 114:240451
TITLE: Pharmacological blockade of chloride pumps or Cl- channels reduces the adenosine-mediated **depression** of stimulus train-evoked calcium fluxes in rat hippocampal slices
AUTHOR(S): Schubert, Peter; Ferroni, Stefano; Mager, Ralph
CORPORATE SOURCE: Dep. Neuromorphol., Max-Planck-Inst. Psychiatry, Martinsried, 8033, Germany
SOURCE: Neuroscience Letters (1991), 124(2), 174-7
CODEN: NELED5; ISSN: 0304-3940
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Stimulus train-evoked decreases of the extracellular Ca2+ concn. (.DELTA.Ca) were measured with ion-sensitive electrodes in the CA1 area of rat hippocampal slices. The adenosine receptor antagonist theophylline led to a marked increase of .DELTA.Ca in the synaptic and in the soma layer reflecting an increased activation and enhanced frequency potentiation of pyramidal neurons in the absence of endogenous adenosine action. The theophylline effect was reduced in the presence of the Cl- channel blocker 4,4'-diisothiocyano-2,2'-stilbenedisulfonate (DIDS) or of the Cl- pump blocker **furosemide**. The data indicate that the adenosine-mediated modulation of the repetitive input strength is related to the function of Cl- ions.

L14 ANSWER 38 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:36337 CAPLUS
DOCUMENT NUMBER: 70:36337
TITLE: Physiological observations on the exocrine pancreas. Effects of some agents on pancreatic secretion
AUTHOR(S): Nakano, Satoshi
CORPORATE SOURCE: Sch. Med., Nagoya Univ., Nagoya, Japan
SOURCE: Nagoya Journal of Medical Science (1968), 31(1), 79-116
CODEN: NJMSAG; ISSN: 0027-7622
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pancreatic secretion studies were performed in dogs and cats under general anesthesia. Pancreatic secretion was maintained by administration of secretin. Following i.v. injection of a synthesized tetrapeptide (I) structurally related to an active part of gastrin a substantial increase of amylase concn. and in amylase output was observed, without any significant change in the other components of the pancreatic juice including electrolytes. Increase in pancreatic juice flow was observed in dogs but not in cats. In human subjects s.c. injection of 300 .mu.g. I after the pancreozymin-secretin combined test resulted in increased juice flow and amylase activity. Injection of serotonin creatinine sulfate (II) resulted in transient **depression** of the juice flow. In dogs the protein content of pancreatic juice increased immediately, but in cats it was either decreased or variable. Hyperventilation and increased motility of the duodenum occurred. In rats multiple gastric ulcers were produced by II. Significant increase of amylase concn. and output in both cats and dogs followed neostigmine administration. There were no significant changes of juice flow or bicarbonate concn. Atropine sulfate did not affect the pancreatic juice flow but inhibited the enhancement of amylase activity by neostigmine. Administration of hyoscine N-butyl bromide (III), a ganglionic blocking agent, was followed by a significant though transient **depression** of pancreatic juice flow. Amylase concn. was slightly increased but amylase output was depressed. In 2 normal human subjects i.v. injection of III resulted in a marked **depression** in juice flow with decrease in amylase activity in one case and a transient **depression** of juice flow without change in amylase activity in the other. Acetazolamide greatly depressed the pancreatic juice flow with a slight **depression** of bicarbonate concn. and an increase in enzyme concn. Na concn. was unchanged but there was a tendency for K concn. to increase. **Furosemide** injection caused a slight **depression** of juice flow and bicarbonate concn. with a slight elevation of protein concn. and a tendency for K concn. to decrease. Following the pancreozymin-secretin combined test, the administration of **furosemide** caused a **depression** of juice flow and elevation of amylase concn. in a normal subject and a slight elevation of amylase concn. in a patient with chronic pancreatitis.

14 ANSWER 33 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1967:63866 CAPLUS
DOCUMENT NUMBER: 66:63866
TITLE: Diuretic therapy of acute intoxication with hypnotics
AUTHOR(S): Krueger, G. A.
CORPORATE SOURCE: Evangelischen Krankenhauses, Muelheim, Fed. Rep. Ger.
SOURCE: Anaesthesist (1967), 16(2), 40-4
CODEN: ANATAE; ISSN: 0003-2417
DOCUMENT TYPE: Journal
LANGUAGE: German

AB **Furosemide** (20 mg.), injected i.v. into patients with barbiturate intoxication and added to running infusions dependent on the progress of the case (an av. of 20 mg./1000 ml.), was an effective therapeutic measure against the intoxication. The drug was easily administered and could be safely used in case of diabetes or complications caused by **depression** of cardiac, circulatory, or liver functions. It considerably reduced the time of unconsciousness and hospital treatment. Circulatory analeptics, particularly ethyldiphenylpropenamine, were effectively used in cases of hypotension in order to reestablish normal blood pressure values. 46 references.

L14 ANSWER 27 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1971:517014 CAPLUS

DOCUMENT NUMBER: 75:117014

TITLE: Oxygen consumption and changes of tissue cation concentrations in K+-depleted rabbit kidney slices, under the influence of diuretic agents, p-chloromercuribenzoate and N-ethylmaleimide

AUTHOR(S): Herms, W.; Kersting, F.

CORPORATE SOURCE: I. Med. Klin., Univ. Duesseldorf, Duesseldorf, Fed. Rep. Ger.

SOURCE: Progr. Nephrol., Proc. Symp. "Ges. Nephrol.", 5th (1969), Meeting Date 1967, 290-5. Editor(s): Peters, Georges. Springer: Berlin, Ger.
CODEN: 23QNA2

DOCUMENT TYPE: Conference

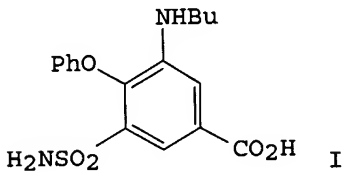
LANGUAGE: English

AB Incubation of rabbit kidney slices with the diuretic agents mersalyl, **hydrochlorothiazide**, **furosemide**, and ethacrynic acid resulted in decreased tissue respiration and increased K+ uptake. The absence of a relationship, however, suggests that active K+ uptake is not closely linked to respiration. An increase in Na+ concn. which did not parallel the **depression** in K+ uptake was also obsd. It is possible that cell membrane permeability might be affected by these agents. Addn. of cysteine chloride partially reversed the effects. A greater protective effect was obsd., however, when the nondiuretic agents, p-chloromercuribenzoate and N-ethyl-maleimide were used.

L14 ANSWER 22 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1971:486492 CAPLUS
DOCUMENT NUMBER: 75:86492
TITLE: Renal and extrarenal factors involved in the hyperuricemia induced by **furosemide**
AUTHOR(S): Schirmeister, J.; Man, N. K.; Hallauer, W.
CORPORATE SOURCE: Med. Universitaetsklin., Freiburg/Br., Fed. Rep. Ger.
SOURCE: Progr. Nephrol., Proc. Symp. "Ges. Nephrol.", 5th (1969), Meeting Date 1967, 59-63. Editor(s): Peters, Georges. Springer: Berlin, Ger.
CODEN: 23QNA2
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Studies were carried out in order to define the renal and extrarenal factors by which **furosemide** modifies the serum uric acid (SUA) concn. The renal effect of **furosemide** in man appears to be 2-fold. First an initial small decrease of urinary urate excretion which could be due to an increased proximal tubular reabsorption of uric acid, enhanced by an increased blood lactate. It is suggested that the 2nd renal effect could be a **depression** of tubular secretion of urate which abolishes the increase in uric acid excretion, expected as a consequence of the augmented uric acid load.

L14 ANSWER 23 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:586781 CAPLUS
DOCUMENT NUMBER: 85:186781
TITLE: Bumetanide, a new loop diuretic
AUTHOR(S): Carriere, S.; Dandavino, R.; Rochefort, F.; Daigneault, A.; Lanoix, C.
CORPORATE SOURCE: Dep. Med., Hop. Maisonneuve-Rosemont, Montreal, QC, Can.
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (1976), 20(4), 424-38
CODEN: CLPTAT; ISSN: 0009-9236
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The effect of bumetanide (I) [28395-03-1] on renal function was compared with that of **furosemide** [**54-31-9**] and a placebo in a double-blind study in 9 healthy young men. The sequence for oral administration of the drug was subjected to a random assignation based upon the Latin-square methodology under these different conditions. During normal hydration the administration of I (2 mg) produced within the next 4 hr a diuresis comparable to that induced by 80 mg of **furosemide**. Urinary excretion of Na, K, Cl, Ca, and uric acid also followed comparable patterns. Phosphaturia occurred only under I. The effect of I seemed longer lasting. During water loading the effects of I and **furosemide** were comparable with the exception of the phosphaturic effect induced by I. The action of both **diuretics** on the diluting segment of the nephron was well demonstrated by the marked **depression** of max. free-water clearance. During water deprivation the effects of the 2 **diuretics** were comparable, including **depression** of max. free-water reabsorption. In none of these

conditions did the placebo produce any significant effect.

L14 ANSWER 24 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:553514 CAPLUS
DOCUMENT NUMBER: 103:153514
TITLE: Nitrogen mustard interference with potassium transport systems in Ehrlich ascites tumor cells
AUTHOR(S): Doppler, Wolfgang; Hofmann, Johann; Oberhuber, Hermann; Maly, Karl; Grunicke, Hans
CORPORATE SOURCE: Inst. Med. Chem. Biochem., Univ. Innsbruck, Innsbruck, A-6020, Austria
SOURCE: Journal of Cancer Research and Clinical Oncology (1985), 110(1), 35-41
CODEN: JCROD7; ISSN: 0171-5216
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nitrogen mustard (N-mustard) [55-86-7] inhibits ouabain [630-60-4]- and **furosemide** [**54-31-9**]-sensitive Rb uptake of Ehrlich ascites tumor cells, whereas the Rb transport resistant to both inhibitors is not affected. Rb transport kinetics served as a congener for the K+-transport in these cells. At N-mustard concns. <10 .mu.M, the redn. in Rb uptake is predominantly due to an interference with the **furosemide**-sensitive system. The dose response curve for the inhibition by N-mustard of the **furosemide**-sensitive Rb uptake closely parallels the dose response curve for the antitumor activity of the alkylating drug. This is in contrast to the behavior of the ouabain-sensitive Rb transport. The inhibition of the **furosemide** -sensitive Rb uptake is expressed much less in cells which are resistant to N-mustard. The recovery of the **furosemide**-sensitive transport system after a single exposure to N-mustard is relatively slow and characterized to an initial 4 h lag period, whereas the repair of DNA-interstrand crosslinks starts immediately after removal of the drug. At millimolar concns., **furosemide** blocks the multiplication of Ehrlich ascites tumor cells. However, lower concns. of **furosemide** which cause a 50% redn. in the **furosemide**-sensitive Rb uptake do not interfere with cell proliferation. This is in contrast to the behavior of N-mustard which exerts a clear-cut **depression** of cell growth at concns. leading to a 50% inhibition of the **furosemide**-sensitive Rb transport transport. It is concluded, that the inhibition of the **furosemide**-sensitive system alone is not sufficient to explain the antitumor activity of the alkylating agent. The effect is discussed as part of a more extended N-mustard-induced membrane alteration which may be important for the growth inhibitory effect of the alkylating agent.

L14 ANSWER 21 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:12436 CAPLUS
DOCUMENT NUMBER: 84:12436
TITLE: Cochlear N1 **depression** produced by the new loop diuretic, bumetanide, in cats
AUTHOR(S): Brown, R. D.
CORPORATE SOURCE: Med. Cent., Louisiana State Univ., Shreveport, LA, USA
SOURCE: Neuropharmacology (1975), 14(8), 547-53
CODEN: NEPHBW; ISSN: 0028-3908
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There was a linear relation between bumetanide (I) [28395-03-1] (1-50 mg/kg, i.v.) and cochlear N1 **depression** in 22 cats. Statistics showed the dose-response curve for I was parallel with other ototoxic **diuretics** and suggested they were acting on the same cochlear sites by the same mechanism. I had an abs. diuretic potency 40-60 times and abs. ototoxic potency .apprx.6.5 times that of **furosemide** (11.92 mg/kg, i.v.).

L14 ANSWER 22 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1971:486492 CAPLUS
DOCUMENT NUMBER: 75:86492
TITLE: Renal and extrarenal factors involved in the hyperuricemia induced by **furosemide**
AUTHOR(S): Schirmeister, J.; Man, N. K.; Hallauer, W.
CORPORATE SOURCE: Med. Universitaetsklin., Freiburg/Br., Fed. Rep. Ger.
SOURCE: Progr. Nephrol., Proc. Symp. "Ges. Nephrol.", 5th (1969), Meeting Date 1967, 59-63. Editor(s): Peters, Georges. Springer: Berlin, Ger.
CODEN: 23QNA2
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Studies were carried out in order to define the renal and extrarenal factors by which **furosemide** modifies the serum uric acid (SUA) concn. The renal effect of **furosemide** in man appears to be 2-fold. First an initial small decrease of urinary urate excretion which could be due to an increased proximal tubular reabsorption of uric acid, enhanced by an increased blood lactate. It is suggested that the 2nd renal effect could be a **depression** of tubular secretion of urate which abolishes the increase in uric acid excretion, expected as a consequence of the augmented uric acid load.

L14 ANSWER 1 OF 106 USPATFULL on STN
ACCESSION NUMBER: 2002:332768 USPATFULL
TITLE: Methods and compositions for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms
INVENTOR(S): Hochman, Daryl W., Seattle, WA, United States
PATENT ASSIGNEE(S): Cytoscan Sciences LLC, Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6495601	B1	20021217	
APPLICATION INFO.:	US 1999-470637		19991222	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-113620P	19981223	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Fay, Zohreh
ASSISTANT EXAMINER: Kwon, Brian Yong S
LEGAL REPRESENTATIVE: Speakman, Ann W., Friedman, Susan J.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 35 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 2851
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and compositions for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms. More specifically, one aspect of the present invention relates to methods and materials for treating seizure and seizure disorders, epilepsy, status epilepticus, **migraine**, spreading **depression**, intracranial hypertension; for treating the pathophysiological effects of head trauma, stroke, ischemia and hypoxia; for treating or protecting from the pathophysiological effects of neurotoxic agents such as ethanol; and for treating neurophsyciatric disorders and central nervous system edema by administering agents that modulate ionic concentrations and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride cotransporter antagonists. Ion-dependent cotransport antagonists and combinations of such compositions with other agents for treating various conditions are disclosed. The present invention also relates to methods and compositions for treating pain by administering ion-dependent cotransporter antagonists. Methods and compositions for enhancing cortical function, for example, in centers of cognition, learning and memory, by administering ion-dependent cotransporter agonists are disclosed. Methods and systems for screening drug candidate compounds for desired activities using in vitro and in vivo systems are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 2 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:508130 CAPLUS
DOCUMENT NUMBER: 83:108130
TITLE: Renal secretion of sulfur-35 labeled-**furosemide** and its **depression** by albumin binding
AUTHOR(S): Bowman, R. H.
CORPORATE SOURCE: VA Hosp., Syracuse, NY, USA
SOURCE: American Journal of Physiology (1975), 229(1), 93-8
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB It was detd. by use of 35S-labeled **furosemide** (I) [**54-31-9**] and an ultrafiltration procedure that **furosemide** is bound extensively to bovine serum albumin. When 500 .mu.moles **furosemide** and albumin at a concn. of 2.5 g/100 ml were used, approx. 90% of the drug was bound. With this same amt. of **furosemide**, but with 3 times as much albumin, binding was about 98%. Using a 25-fold lower concn. of **furosemide**, 20 .mu.moles, binding was nearly 98% with 2.5 g albumin/100 ml, and was over 98% with 7.5 g albumin/100 ml. These same concns. of **furosemide** and albumin were used to investigate the excretory and secretory rates of 35S-labeled **furosemide** in the isolated perfused rat kidney. Tubular clearance (i.e., secretion) of **furosemide** was inversely related to the concn. of albumin in the perfusate. In kidneys perfused without albumin, tubular clearance of the drug was 6-20 times that found when 2.5 or 7.5 g albumin/100 ml, resp., was used. Probenecid, with or without albumin, reduced the clearance of **furosemide** to that of its filtration rate. Thus, at physiol. albumin concns., a very small fraction of circulating **furosemide** will be available for filtration, and tubular-fluid and urinary **furosemide** will arise predominantly from secretion. Because of extensive binding of **furosemide** to albumin, the renal secretory process itself would be depressed, and the rate of secretion will be dependent, in part, on the concn. of unbound drug.

L14 ANSWER 3 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1982:97452 CAPLUS

DOCUMENT NUMBER: 96:97452

TITLE: Comparative acute cochlear toxicity of intravenous bumetanide and **furosemide** in the purebred beagle

AUTHOR(S): Brown, R. Don

CORPORATE SOURCE: Sch. Med., Louisiana State Univ., Shreveport, LA, 71130, USA

SOURCE: Journal of Clinical Pharmacology (1981), 21(11-12, Pt. 2), 620-7
CODEN: JCPCBR; ISSN: 0091-2700

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Comparisons were made of the effects of various doses of i.v. bumetanide [28395-03-1] and **furosemide** [**54-31-9**] on the primary auditory afferent activity (N1) and cochlear microphonics (CM) of beagles. The dose-response relations of the N1 **depressions** to bumetanide and **furosemide** are parallel; those of the CM **depressions** are also parallel but have a much shallower slope than those of the N1 **depressions**. With both drugs, N1 **depression** occurs at lower doses than does CM **depression**. The N1 **depression** produced by a particular dose of bumetanide or **furosemide** bore a linear relation to the CM **depression** produced. This finding supports the postulate that the cochlear site and mechanism of ototoxic action of the loop **diuretics** are directed at an earlier step of the cochlear transduction process than N1. Using N1 **depression** as the gross electrophysiol. index of ototoxicity, the acute ototoxic potency of bumetanide in beagles is .apprx.6.5 times that of **furosemide**, whereas its diuretic potency is 40-60 times that of **furosemide**. Therefore, when clin. dosages of the 2 drugs are considered, the relative acute ototoxic potency of bumetanide in the beagle is 0.11-0.16 that of **furosemide**. This range is identical to the relative ototoxic potency of 0.11-0.16 previously obtained in the cat. Serum concns. of bumetanide and **furosemide** increased linearly with the doses of the 2 drugs, except for the highest dose given (100 mg/kg for both drugs). The serum concns. at that dose of both drugs are less than the math. predicted values. Histol. (light-microscopic) examn. of the cochleas did not reveal any significant pathol.

L14 ANSWER 4 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:53966 CAPLUS
DOCUMENT NUMBER: 70:53966
TITLE: Effects of **diuretics** on respiration and changes in tissue sodium and potassium concentrations
AUTHOR(S): Herms, Wolfgang; Kersting, Friedhelm
CORPORATE SOURCE: I Med. Klin., Univ. Duesseldorf, Duesseldorf, Fed. Rep. Ger.
SOURCE: Zeitschrift fuer die Gesamte Experimentelle Medizin (1969), 149(1), 13-24
CODEN: ZGEMAZ; ISSN: 0372-8722
DOCUMENT TYPE: Journal
LANGUAGE: German
AB O consumption and restoration of K+ by K+-depleted rabbit kidney cortical slices were studied in incubation media contg. p-chloromercuribenzoate (4 .times. 10-4 moles/l.), N-ethylmaleimide (10-4 moles/l.), and the diuretic agents, mersalyl (200-800 mg./l.), **hydrochlorothiazide** (100-400 mg./l.), **furosemide** (40-320 mg./l.), and ethacrynic acid (40-320 mg./l.). With increasing doses of all compds. tested, a decrease in O consumption, a decrease in K+ restoration, and an increase in tissue Na+ concn. were observed as compared with controls. No correlation between the **depression** rate of respiration and the decrease in K+ uptake was observed, except with **hydrochlorothiazide**. With **furosemide** and ethacrynic acid, the decrease in O consumption was proportionately higher than the decrease in K+ restoration, whereas with mersalyl, the inhibition of K+ uptake paralleled the inhibition of respiration. No relation between the changes in K+ concns. and reciprocal Na+ concns. was observed. The increase in tissue Na+ was relatively higher than the decrease in K+ restoration, as compared with controls, esp. with ethacrynic acid, suggesting an addnl. effect on a K+ and O insensitive Na+ pump. Cysteine chloride, added at twice the molar concn., reversed the effect of N-ethylmaleimide on tissue respiration and on the Na+ and K+ ion concns., but had only minor effects on p-chloromercuribenzoate, **hydrochlorothiazide**, and mersalyl, and almost no effect on **furosemide** induced changes.

L14 ANSWER 5 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:191432 CAPLUS
DOCUMENT NUMBER: 112:191432
TITLE: The influence of **furosemide** on plasma elimination and urinary excretion of drugs in standardbred horses
AUTHOR(S): Stevenson, A. J.; Weber, M. P.; Todi, F.; Mendonca, M.; Fenwick, J. D.; Kwong, E.; Young, L.; Leavitt, R.; Nespolo, R.; et al.
CORPORATE SOURCE: Race Track Div., Agric. Canada, Ottawa, ON, K2C 3X7, Can.
SOURCE: Journal of Veterinary Pharmacology and Therapeutics (1990), 13(1), 93-104
CODEN: JVPTD9; ISSN: 0140-7783
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of i.v. administration of 150 or 250 mg of **furosemide** to standardbred mares pre-treated with 9 other drugs were studied. **Furosemide** reduced the plasma concns. of codeine compared to control 2-6 h after **furosemide** administration. The plasma concns. of theophylline, phenylbutazone, pentazocine, guaifenesin, and flunixin were not markedly altered by **furosemide**. In the case of acepromazine, clenbuterol, and fentanyl, the data generated were insufficient. A significant redn. was noted in the urinary concns. of guaifenesin, acepromazine, clenbuterol, phenylbutazone, flunixin, fentanyl, and pentazocine within 1-4 h of **furosemide** administration. The urinary concns. of theophylline remained reduced as

long as 8 h after **furosemide** injection. **Furosemide** administration to horses pre-treated with codeine resulted in **depression** of urinary morphine concns. 2-4 h and 9-12 h after **furosemide** injection. A lower **furosemide** dose produced changes in drug urinary excretion and plasma elimination equiv. to the higher dose. Thus, **furosemide** affects the urinary and plasma concns. of other co-administered drugs but not in a predictable fashion, which limits the extrapolation of these results to as yet untested drugs.

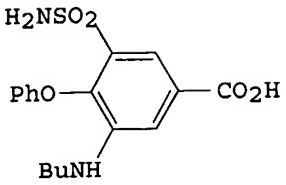
L14 ANSWER 6 OF 106 USPATFULL on STN
ACCESSION NUMBER: 2003:11156 USPATFULL
TITLE: Treatment of congestive heart failure
INVENTOR(S): Bakker-Arkema, Rebecca Guggemos, Ann Arbor, MI, UNITED STATES
Pressler, Milton Lethan, Saline, MI, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003008860	A1	20030109	
APPLICATION INFO.:	US 2002-129892	A1	20020509	(10)
	WO 2001-US9265		20010322	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Charles W Ashbrook, Warner Lambert Company, 2800 Plymouth Road, Ann Arbor, MI, 48105
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 856
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Combinations of **diuretics** and vasopressin antagonists are useful to slow and reverse the symptoms and process of congestive heart failure, to increase the excretion of water in the urine, and to decrease the excretion of sodium and potassium ions in urine. Preferred vasopressin antagonists have the formula (I) wherein R and R.sup.5 are hydrogen or lower alkyl; R.sup.1, R.sup.2, and R.sup.3 are hydrogen, halo, alkyl, alkoxy, and amino; and R.sup.4 is hydrogen or phenyl, and a pharmaceutically acceptable salt thereof

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 7 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1979:449579 CAPLUS
DOCUMENT NUMBER: 91:49579
TITLE: Comparative acute ototoxicity of intravenous bumetanide and **furosemide** in the pure-bred beagle
AUTHOR(S): Brown, R. Don; Manno, Joseph E.; Daigneault, Ernest A.; Manno, Barbara R.
CORPORATE SOURCE: Sch. Med. Shreveport, Louisiana State Univ., Shreveport, LA, 71130, USA
SOURCE: Toxicology and Applied Pharmacology (1979), 48(1, Pt. 1), 157-69
CODEN: TXAPA9; ISSN: 0041-008X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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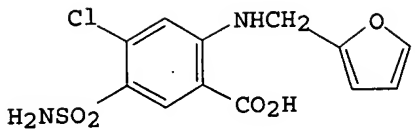


II

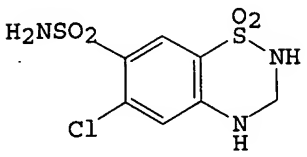
AB The effects of various doses of i.v. bumetanide (I) [28395-03-1] and **furosemide** (II) [**54-31-9**] on the auditory afferent activity (N1) and cochlear microphonics (CM) of beagles were detd. in a quant. manner. Serum concns. of these 2 loop **diuretics** were also detd. at 3.5 min after the injections in the majority of the animals. The dose-response relationships of the N1 **depressions** to I and II were parallel; those of the CM **depressions** were also parallel but had a much shallower slope than those of the N1 **depressions**. With both drugs, N1 **depression** occurred at lower doses than did CM **depression**. When multiple linear regression anal. was performed, the N1 **depression** produced by a particular dose of I or II bore a linear relationship to the CM **depression** produced. Thus, the cochlear site and mechanism of ototoxic action of the loop **diuretics** were directed at an earlier step of the cochlear transduction process than N1. Serum concns. of I and II increased linearly with the doses of the 2 drugs, except for the highest dose given (100 mg/kg for both drugs). The serum concns. at the dose of both drugs were lower than the math. predicted values. Histol. examn. of the cochleas did not reveal any significant pathol. changes produced in the stria vascularis, outer and inner hair cells, afferent and efferent nerve terminals, or the spiral ganglia and efferent nerve bundles. Using N1 **depression** as the gross electrophysiologic index of ototoxicity, the acute ototoxic potency of I in beagles was .apprx.6.5 times that of II, whereas its diuretic potency was 40-60 times that of II. Therefore, when clin. dosages of the 2 drugs were considered, the relative, acute ototoxic potency of I in the beagle was 0.11-0.16 that of II. This range was identical to the relative ototoxic potency of 0.11-0.16 previously obtained in the cat.

L14 ANSWER 8 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1973:474270 CAPLUS
DOCUMENT NUMBER: 79:74270
TITLE: Diuretic **depression** of fluorescein secretion in the proximal tubules of frog kidney. Vital examination by contact microscopy
AUTHOR(S): Bresler, V. M.; Natochin, Yu. V.
CORPORATE SOURCE: I. M. Sechanov Inst. Evol. Physiol. Biochem., Leningrad, USSR
SOURCE: Byulleten Eksperimental'noi Biologii i Meditsiny (1973), 75(6), 67-9
CODEN: BEBMAE; ISSN: 0365-9615
DOCUMENT TYPE: Journal
LANGUAGE: Russian

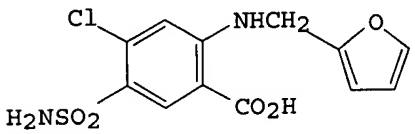
AB Frog kidney proximal tubule cells intensely secreted fluorescein [2321-07-5] after administration of the compd. in vivo or to an isolated kidney. The **diuretics furosemide** (I) [**54-31-9**], ethacrynic acid [58-54-8], triampur(triamterene) [396-01-0], brinaldix [636-54-4], and an aldactone-saltucin mixt. [39394-35-9], administered in doses which prevented Na resorption, inhibited the passage of fluorescein through the apical membrane and the lumen of the proximal tubules, but did not affect fluorescein accumulation in the cells of the tubules. Apparently the **depression** of fluorescein secretion by the **diuretics** was due to the effects of the compds. on the system of Na transport located in the apical plasmatic membrane of the proximal

tubules.

L14 ANSWER 9 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:202614 CAPLUS
DOCUMENT NUMBER: 94:202614
TITLE: The role of intrarenal prostaglandin E in the action of **diuretics**
AUTHOR(S): Dagher, Georges; Berbari, Adel
CORPORATE SOURCE: Hop. Necker, Paris, 75015, Fr.
SOURCE: Developments in Endocrinology (Amsterdam) (1980), 10(Horm. Regul. Sodium Excretion), 213-20
CODEN: DENDD4; ISSN: 0165-1900
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB In rats, **hydrochlorothiazide** (I) [58-93-5] and **furosemide** (II) [**54-31-9**] induced a diuresis and natriuresis of similar magnitude with no change in plasma or renal PGE levels. The diuretic response following I in indomethacin-treated rats was less marked, and was assocd. with a redn. in plasma and renal PGE levels. Na or K excretions were unchanged. The potentiation of II-induced diuresis and natriuresis by indomethacin was assocd. with a **depression** in renal prostaglandins. Indomethacin treatment inhibited hyperreninemia of II-treated rats. Apparently, intrarenal PGE plays a role in the mechanism of II diuresis and natriuresis in the rat.

L14 ANSWER 10 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1970:475301 CAPLUS
DOCUMENT NUMBER: 73:75301
TITLE: Ototoxicity of new and potent **diuretics**
AUTHOR(S): Mathog, Robert H.; Thomas, William G.; Hudson, William R.
CORPORATE SOURCE: Med. Center, Duke Univ., Durham, NC, USA
SOURCE: Archives of Otolaryngology (1970), 92(1), 7-13
CODEN: AROTAA; ISSN: 0003-9977
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ethacrynic acid and **furosemide** produced a primary **depression** of the cochlear microphonic and action potential in cats; complete recovery ensued within 1 hr. A secondary **depression** with outer hair cell degenearation in the basal and middle coils of the cochlea was obsd. after high doses of ethacrynic acid.

L14 ANSWER 11 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1967:54072 CAPLUS
DOCUMENT NUMBER: 66:54072
TITLE: Action of **diuretics** in dogs studied by micropuncture
AUTHOR(S): Berliner, Robert W.; Dirks, John H.; Cirksena, William J.
CORPORATE SOURCE: Natl. Health Inst., Bethesda, MD, USA
SOURCE: Annals of the New York Academy of Sciences (1966), 139(2), 424-32

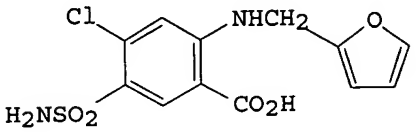
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Depressed reabsorption in the accessible portion of the proximal tubule of the dog kidney contributed to the diuresis which followed the administration of **hydrochlorothiazide** (2 mg./kg.), **furosemide** (5 and 25 mg./kg.), chlormerodrin (2 mg./kg.), and ethacrynic acid (1 and 5 mg./kg.). The effects of infusing isotonic saline soln., detected as a **depression** of reabsorption in the proximal convoluted tubule, were assocd. with greater reabsorption of Na salts and H2O in the loop of Henle and beyond, than previously thought. These amts. were large enough to explain the magnitude of the diuresis involved.

L14 ANSWER 12 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1970:65055 CAPLUS
DOCUMENT NUMBER: 72:65055
TITLE: Effect of **furosemide** on sodium and potassium ion transport studied by microperfusion of the rat nephron
AUTHOR(S): Morgan, Trefor; Tadokoro, Masao; Martin, Denis G.; Berliner, Robert W.
CORPORATE SOURCE: Nat. Heart Inst., Nat. Inst. of Health, Bethesda, MD, USA
SOURCE: American Journal of Physiology (1970), 218(1), 292-7
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Proximal tubules, loops of Henle, and distal tubules were perfused with a soln. contg. **furosemide** (1-10 mg/l.) and the net transport of Na+ and K+ was compared with that obtained during control perfusions. In addn., the ability of the proximal tubule to create a gradient for Na+ when raffinose was in the perfusate was detd. in the presence and absence of **furosemide**. Net Na absorption in the proximal tubule as measured by water absorption decreased from 1.31 .+-. 0.07 to 0.77 .+-. 0.14 nl./min/mm. The concn. difference developed in the presence of raffinose fell from 2 4.3 .+-. 0.8 to 15.3 .+-. 0.9 mequiv./l. when **furosemide** was present. Net absorption by the loop of Henle decreased from 1.79 to 0.85 nequiv./m in for Na and from 0.034 to -0.009 nequiv./min for K. No **depression** of Na transport was detected in the distal tubule. Although K entered the perfusate in the distal tubule, it was difficult t o det. whether the rate of entry was affected by **furosemide**. The changes obsd. appear to account for the pattern of Na and K excretio n of urine.

L14 ANSWER 13 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:631010 CAPLUS
DOCUMENT NUMBER: 93:231010
TITLE: Interaction of conventional and antikaliuretic **diuretics** with the renal prostaglandin system
AUTHOR(S): Kramer, H. J.; Duesing, R.; Stinnesbeck, B.; Prior, W.; Baecker, Angela; Eden, Jutta; Kipnowski, J.; Glaenzer, K.; Krueck, F.
CORPORATE SOURCE: Poliklin., Med. Univ., Bonn, Fed. Rep. Ger.
SOURCE: Clinical Science (1980), 59(1), 67-70
CODEN: CSCIAE; ISSN: 0143-5221
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Urinary excretion of PGE2 [363-24-6] was increased from 1.24 to 2.60, 2.93, and 4.28 mmol/24 h by frusemide [**54-31-9**], **hydrochlorothiazide** (I) [58-93-5], and spironolactone [52-01-7], resp. A rise in PGF2.alpha. [551-11-1] induced by I was quant. similar but statistically insignificant. I- and frusemide-induced Na excretion was reduced by indomethacin [53-86-1] as was spironolactone-induced K

sparing and the rise in plasma renin [9015-94-5] obsd. with all 3 **diuretics**. Indomethacin enhanced urinary osmolality and free water absorption in the presence of spironolactone but not I or frusemide. Thus, increased prostaglandin activity after **diuretics** may contribute to their natriuretic action; this and the antikaliuretic effect of spironolactone may be partially abolished by nonsteroidal antiphlogistic agents.

L14 ANSWER 14 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1978:15724 CAPLUS
DOCUMENT NUMBER: 88:15724
TITLE: Effects of **furosemide** on glomerular filtration rate and clearance of practolol, digoxin, cephaloridine, and gentamicin
AUTHOR(S): Tilstone, W. J.; Semple, P. F.; Lawson, D. H.; Boyle, J. A.
CORPORATE SOURCE: Dep. Pharm. Chem., Univ. Strathclyde, Glasgow, UK
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (1977), 22(4), 389-94
CODEN: CLPTAT; ISSN: 0009-9236
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

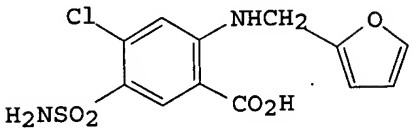


I

AB **Furosemide** (I) [**54-31-9**] decreased inulin clearance in 20 of 27 normal subjects. The **depression** in inulin clearance occurred in both water-loaded and non-water-loaded subjects. The renal clearance of practolol [6673-35-4], but not digoxin [20830-75-5], was reduced when I was given. The av. total plasma clearances of gentamicin [1403-66-3] and cephaloridine [50-59-9] over a 6-h period were decreased after I. The reduced clearances of the antibiotics were assocd. with higher plasma levels, the increase in antibiotic concn. being as much as 100% at 1 h after an i.v. bolus injection.

L14 ANSWER 15 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:207410 CAPLUS
DOCUMENT NUMBER: 106:207410
TITLE: Effects of dipyridamole and **furosemide** on renal function during adenine infusion in rats
AUTHOR(S): Redlak, Maria; Szczepanska-Konkel, Miroslawa; Stepinski, Jan; Angielski, Stefan
CORPORATE SOURCE: Zakl. Biochem. Klin., Akad. Med., Gdansk, 80-227, Pol.
SOURCE: Acta Physiologica Polonica (1986), 37(1), 1-7
CODEN: APYPAY; ISSN: 0044-6033
DOCUMENT TYPE: Journal
LANGUAGE: English
AB I.v. infusion of NAD [53-84-9] (200 nmole/kg/min) to rats decreased urine flow, renal plasma flow, glomerular filtration rate, and urinary excretion of Na+ and adenosine (I) [58-61-7] but increased plasma I concn. Infusion of NAD (50 nmole/kg/min) or dipyridamole [58-32-2] (25 .mu.g/h/min) affected neither renal function nor plasma I levels but infusion of the agents together depressed renal function and raised plasma I. **Furosemide** [**54-31-9**] failed to abolish the renal function **depression** induced by NAD.

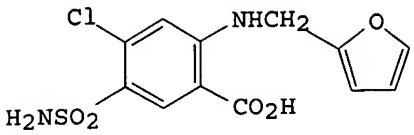
L14 ANSWER 16 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:96176 CAPLUS
DOCUMENT NUMBER: 94:96176
TITLE: Pharmacologic determinants of ototoxicity of **furosemide** in the chinchilla
AUTHOR(S): Green, Thomas P.; Rybak, Leonard P.; Mirkin, Bernard L.; Juhn, S. K.; Morizono, Tetsuo
CORPORATE SOURCE: Dep. Pharmacol., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1981), 216(3), 537-42
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB In chinchillas 15 min after the administration of an ototoxic dose of **furosemide** (I) [**54-31-9**] (100 mg/kg, i.v.) the highest concn. of I was found in perilymph. Elimination of the drug from perilymph paralleled that from serum, and a 65:1 drug concn. gradient (serum/perilymph) was rapidly established and maintained. The same gradient was found after other ototoxic I doses (25-200 mg/kg) and after chronic I administration. The magnitude of this gradient could not be accounted for by binding of I to serum proteins, by pH-dependent drug partitioning or by cochlear drug glucuronidation. The drug elimination profile from perilymph was most consistent with free penetration of drug into the inner ear coupled with rapid removal. The time course of endocochlear potential **depression** was strikingly similar to the I-perilymph concn. time curve; maximal endocochlear potential **depression** occurred at 5 to 15 min following the i.v. dose, corresponding with the time of peak perilymph I levels, but not with local diuretic effects on electrolytes. Calcns. based on the pharmacokinetic data revealed that I produced **depression** of endocochlear potential only at doses sufficient to produce I perilymph concns. >1.3 .mu.g/mL. Furthermore, this potential remained depressed only as long as the local I concn. exceeded this same threshold value. Apparently, the ototoxicity of I is related directly to drug penetration rather than mediated through secondary effects on electrolytes.

L14 ANSWER 17 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1983:11226 CAPLUS
DOCUMENT NUMBER: 98:11226
TITLE: Effects of **furosemide** on the neuromuscular junction
AUTHOR(S): Scappaticci, K. A.; Ham, J. A.; Sohn, Y. J.; Miller, R. D.; Dretchen, K. L.
CORPORATE SOURCE: Sch. Med. Dent., Georgetown Univ., Washington, DC, 20007, USA
SOURCE: Anesthesiology (1982), 57(5), 381-8
CODEN: ANESAV; ISSN: 0003-3022
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The effects of **furosemide** (I) [**54-31-9**] on neuromuscular transmission were studied using the in vitro rat phrenic nerve diaphragm and the in vivo cat soleus nerve muscle prepns. I (10-6-10-4 M) reduced the concn. of d-tubocurarine required to achieve 50% twitch tension **depression** in the indirectly stimulated rat diaphragm. Intraarterial injection of I had a biphasic effect on the cat neuromuscular junction. At low doses (0.1-10.0 .mu.g/kg) the drug had a depressant effect, reduced the force of muscle contraction, prevented nerve and muscle responses to NaF and dibutyryl cyclic AMP, and intensified the neuromuscular blockade produced by d-tubocurarine and succinylcholine. In contrast, in higher doses (1-4 mg/kg) I produced stimulus-bound repetitive neural activity, initiated neural activity, increased the force of muscle contraction, enhanced nerve and muscle responses to NaF and dibutyryl cyclic AMP, and antagonized d-tubocurarine and succinylcholine blockades. I had no effect on denervated prepns. High doses of I inhibit noncompetitively both the high- and low-affinity forms of the enzyme cyclic AMP phosphodiesterase in both sol. and particulate fractions of cat sciatic nerve. Thus, I has direct effects on neuromuscular transmission, but the direction of these effects is dose-dependent.

L14 ANSWER 18 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:522273 CAPLUS
DOCUMENT NUMBER: 109:122273
TITLE: Lithium clearance as an indicator of proximal tubular sodium handling during **furosemide** diuresis
AUTHOR(S): Christensen, Sten; Shalmi, Michael; Petersen, Joergen S.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Copenhagen, Copenhagen, DK-2100, Den.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1988), 246(2), 753-7
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate the use of the renal Li clearance as an indicator of proximal tubular Na handling during **furosemide** diuresis, clearance expts. were performed in conscious catheterized rats. Maximal **depression** of proximal Na reabsorption was induced by isotonic saline expansion (40 mL/h) and under these conditions **furosemide** (7.5 mg/kg/h) did not increase abs. or fractional clearance of Li. These results provide indirect evidence against the existence of a **furosemide** -sensitive Li reabsorption in the ascending limb of Henle. The increase of abs. and fractional Li clearance obsd. in nonexpanded animals given **furosemide** therefore most likely reflects inhibition of electrolyte reabsorption in the proximal tubules. Using Li clearance as a measure for Na output from the proximal tubules, the study provided information about the contribution of proximal and distal nephron segments to saline expansion natriuresis. Apparently, the natriuresis is caused by enhanced delivery of Na from the proximal tubules, which is only partially compensated for by a load-dependent increase of abs. distal Na reabsorption, most likely occurring in the thick ascending limb of Henle.

L14 ANSWER 19 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:422347 CAPLUS
DOCUMENT NUMBER: 83:22347

TITLE: Comparison of the cochlear toxicity of sodium ethacrynate, **furosemide**, and the cysteine adduct of sodium ethacrynate in cats
AUTHOR(S): Brown, R. Don
CORPORATE SOURCE: Sch. Med., Louisiana State Univ., Shreveport, LA, USA
SOURCE: Toxicology and Applied Pharmacology (1975), 31(2), 270-82
CODEN: TXAPA9; ISSN: 0041-008X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The durations of the N1 **depression** in anesthetized cats produced by i.v. administration of Na ethacrynate (I) [6500-81-8] (5.0 mg/kg) and the cysteine adduct of Na ethacrynate (II) [51246-37-8] (2.4 mg/kg) were much longer than that produced by **Furosemide** (III) [**54-31-9**] (12.0 mg/kg). However, the dose-response curves for I, II and III were parallel with II having the greatest potency followed by I and then III. The dose-time to max. effect curves were also parallel with II being the fastest followed by III and then I, which had an irreducible latent period. Thus, all 3 agents appear to produce ototoxicity by acting on the same cochlear site by the same mechanism of action. The difference in duration of N1 **depression** were probably due to I and II not diffusing out of the cochlea as readily as III, or to III beingn inactivated by cochlear tissue. Also, I may be converted partly or wholly to II before exerting an ototoxic effect.

L14 ANSWER 20 OF 106 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1977:593958 CAPLUS
DOCUMENT NUMBER: 87:193958
TITLE: Effects of some **diuretics** and metabolic inhibitors on the sodium transport and electrical properties of the intestinal mucous membrane of the rat in situ
AUTHOR(S): Shida, Masaru; Kikuchi, Shintaro
CORPORATE SOURCE: Cent. Res. Div., Takeda Chem. Ind. Ltd., Osaka, Japan
SOURCE: Takeda Kenkyushoho (1977), 36(1-2), 53-63
CODEN: TAKHAA; ISSN: 0371-5167
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The rat small intestine at the transitional part between the jejunum and ileum was suspended in situ in physiol. saline at 32 to 34.degree. and the transepithelial p.d. (PD), short circuit current (SCC) and sp. resistance (Re) were recorded to give the values 3 to 11 mV, 37 to 142 .mu.A/cm2 and 38 to 204 .OMEGA..cm2, resp. Addn. of 3 .times. 10-3 M NaCN to the intraluminal fluid, composed of 10 mM glucose and 145 mM NaCl, depressed the Na influx across the mucous membrane by 47%, assocd. with **depression** of the transepithelial PD and SCC equally by about 60%. A similar **depression** of the Na influx caused by addn. of 10-3 M 2,4-dinitrophenol [51-28-5] or 10-3 M iodoacetic acid [64-69-7] was accompanied by **depression** of the PD and ACC by about 20%. The transepithelial Re was not changed by the addn. of these metabolic inhibitors. The intraluminal administration of **diuretics** also depressed concn.-dependently the Na influx. The relatively similar **depression** of the Na influx by 35 to 45% caused by **hydrochlorothiazide** [58-93-5], amiloride [2609-46-3], or 10-3 M DS-511 [1,4-dimorpholino-7-phenylpyrido[3,4-d]pyridazine] [39632-88-7] was accompanied by the decrease of the SCC by 13, 11 and 24% but by the increase of the transepithelial PD was not significantly affected by any of these **diuretics**. **Furosemide** [**54-31-9**] (6 .times. 10-4 M) depressed the Na influx, PD, SCC and Re by 39, 32, 19 and 15%, resp. Acetazolamide [59-66-5] (10-3 M) depressed only the Na influx and SCC by 23 and 6%, resp. None of the metabolic inhibitors or the **diuretics**, when applied serosally in physiol. saline at the corresponding concn., nor the **diuretics** injected i.v. affected

the Na influx or the elec. properties of the mucous membrane.

(FILE 'HOME' ENTERED AT 16:06:01 ON 03 OCT 2003)

FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 16:06:14 ON 03 OCT 2003

L1	58209	S 54-31-9/RN OR FUROSEMIDE
L2	23161	S ACETAZOLAMIDE OR DIAMOX
L3	141415	S MIGRAINE OR HEADACHE
L4	486	S L1 AND L3
L5	622	S L2 AND L3
L6	445	DUP REM L4 (41 DUPLICATES REMOVED)
L7	449	DUP REM L5 (173 DUPLICATES REMOVED)
L8	52	S L6 AND MIGRAINE
L9	52	FOCUS L8 1-

=>

L9 ANSWER 15 OF 52 MEDLINE on STN
ACCESSION NUMBER: 1998114015 MEDLINE
DOCUMENT NUMBER: 98114015 PubMed ID: 9453270
TITLE: **Furosemide** inhibits regenerative cortical spreading depression in anaesthetized cats.
AUTHOR: Read S J; Smith M I; Benham C D; Hunter A J; Parsons A A
CORPORATE SOURCE: Neurosciences Research, SmithKline Beecham Pharmaceuticals, Harlow, Essex, UK.
SOURCE: CEPHALALGIA, (1997 Dec) 17 (8) 826-32.
Journal code: 8200710. ISSN: 0333-1024.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980319
Last Updated on STN: 19980319
Entered Medline: 19980310

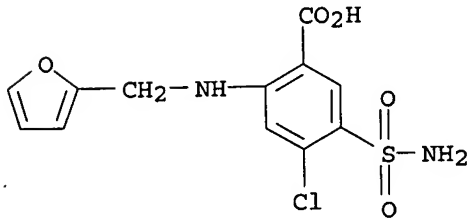
AB Ionic perturbations occur during cortical spreading depression (SD), a phenomenon implicated in **migraine** pathophysiology. We studied the effect of 0.2, 2 and 20 mg kg-1 i.v. (n=4) **furosemide** on cortical direct current (d.c.) potential, cerebrovascular laser Doppler flux (rCBF[LDF]), artery diameter and NO concentration in the parietal cortex of the anaesthetized cat during repetitive SD. In vehicle-treated animals (n=4), SD activity was sustained for 50+/-1.8 min. However, duration of SD activity was significantly reduced when compared to vehicle to 39+/-6.6 (n=4), 34+/-8.5 (n=4) and 27.3+/-11.3 min (n=4), at 0.2, 2 and 20 mg kg-1 i.v. **furosemide** respectively. It is hypothesized that the mechanism of inhibition of SD d.c. activity by **furosemide** may be through alterations in cortical ion buffering capacity or inhibition of cell swelling in neurones or glia. These mechanisms may represent potential novel drug targets in future **migraine** therapy.

L9 ANSWER 32 OF 52 MEDLINE on STN

ACCESSION NUMBER: 2000497652 MEDLINE
DOCUMENT NUMBER: 20438668 PubMed ID: 10980751
TITLE: Treatment of a prolonged migrainous aura with intravenous **furosemide**.
AUTHOR: Rozen T D
CORPORATE SOURCE: Jefferson Headache Center/Thomas Jefferson University Hospital, Philadelphia, PA 19107, USA..
tood.rozen@mail.tju.edu
SOURCE: NEUROLOGY, (2000 Sep 12) 55 (5) 732-3.
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001016

10 ANSWER 20 OF 20 REGISTRY COPYRIGHT 2003 ACS on STN
RN 54-31-9 REGISTRY
CN Benzoic acid, 5-(aminosulfonyl)-4-chloro-2-[(2-furanylmethyl)amino]- (9CI)
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Anthranilic acid, 4-chloro-N-furfuryl-5-sulfamoyl- (8CI)
OTHER NAMES:
CN 2-Furfurylamino-4-chloro-5-sulfamoylbenzoic acid
CN 4-Chloro-N-(2-furylmethyl)-5-sulfamoylanthranilic acid
CN 4-Chloro-N-furfuryl-5-sulfamoylanthranilic acid
CN 5-(Aminosulfamyl)-4-chloro-2-[(2-furanylmethyl)amino]benzoic acid
CN Aisemide
CN Aldic
CN Aluzine
CN Anfuramaide
CN Apo-Frusemide
CN **Apo-Furosemide**
CN Aquamide
CN Aquarid
CN Aquasin
CN Arasemide
CN Beronald
CN Bioretic
CN Cetasix
CN Desdemin
CN Dirine
CN Disal
CN Discoid
CN Disemide
CN Diural
CN Diuresal
CN Diuretic salt
CN Diurin
CN Diurolasa
CN Diusemide
CN Diusil
CN Dranex
CN Dryptal
CN Durafurid
CN Edenol
CN Errolon
CN Eutensin
CN Fluidrol
CN Franyl
CN Frumex
CN Frumide
CN Frusedan
CN Frusema
CN Frusemide
CN Frusemin
CN Frusetic
CN Frusid
CN Fulsix
CN Fuluvamide
CN Furanthril
CN Furanthryl
CN **Furosemide**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
DISPLAY
FS 3D CONCORD
MF C12 H11 Cl N2 O5 S
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,

CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4916 REFERENCES IN FILE CA (1907 TO DATE)
51 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4927 REFERENCES IN FILE CAPLUS (1907 TO DATE)
66 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

L2 ANSWER 1 OF 1 USPATFULL on STN

ACCESSION NUMBER: 2002:332768 USPATFULL

TITLE: Methods and compositions for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms

INVENTOR(S): Hochman, Daryl W., Seattle, WA, United States

PATENT ASSIGNEE(S): Cytoscan Sciences LLC, Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6495601	B1	20021217	<--
APPLICATION INFO.:	US 1999-470637		19991222	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-113620P	19981223 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Fay, Zohreh

ASSISTANT EXAMINER: Kwon, Brian Yong S

LEGAL REPRESENTATIVE: Speakman, Ann W., Friedman, Susan J.

NUMBER OF CLAIMS: 6

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 35 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 2851

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods and compositions for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms. More specifically, one aspect of the present invention relates to methods and materials for treating seizure and seizure disorders, epilepsy, status epilepticus, migraine, spreading depression, intracranial hypertension; for treating the pathophysiological effects of head trauma, stroke, ischemia and hypoxia; for treating or protecting from the pathophysiological effects of neurotoxic agents such as ethanol; and for treating neurophsyciatric disorders and central nervous system edema by administering agents that modulate ionic concentrations and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride cotransporter antagonists. Ion-dependent cotransport antagonists and combinations of such compositions with other agents for treating various conditions are disclosed. The present invention also relates to methods and compositions for treating pain by administering ion-dependent cotransporter antagonists. Methods and compositions for enhancing cortical function, for example, in centers of cognition, learning and memory, by administering ion-dependent cotransporter agonists are disclosed. Methods and systems for screening drug candidate compounds for desired activities using in vitro and in vivo systems are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Drug screening

IT Epilepsy

IT Hypoxia, animal

IT Ischemia

IT Mental disorder

IT Seizures
(Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)

IT Biological transport
(cation-chloride cotransporter antagonist; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)

IT Nervous system
(central, disease, including edema and cortical function disorder; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Brain
(cerebral cortex, spreading depression; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Cognition
IT Learning
IT Memory, biological
(disorder treatment; Methods and compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Animal
IT Animal tissue culture
IT Organ, animal
(for drug screening; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Hypertension
(intracranial; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Neuroglia
(ion-dependent cotransporter antagonist highly active in; Methods and compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Diuretics
(loop, in combination with anti-seizure compn.; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Headache
(migraine; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Toxicity
(neurotoxicity; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Nervous system
(peripheral, disorders; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Epilepsy
(status epilepticus; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Brain, disease
(stroke; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Nerve
(toxicity; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Head
(trauma; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)
IT Pain
(treatment; Methods and compds. for treating central and peripheral

nervous system disorders and methods for screening the compds.)

IT 50-06-6, Phenobarbital, biological studies
(as anti-seizure compn., in combination with ion-dependent cotransporter; Methods and compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)

IT 54-31-9
(in combination with anti-seizure compn.; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)

IT 50-11-3, Metharbital 50-12-4, Mephenytoin 57-41-0, Phenytoin 63-98-9, Phenacemide 67-52-7D, 2,4,6(1H,3H,5H)-Pyrimidinetrione, derivs. 76-74-4, Pentobarbital 76-75-5, Thiopental 77-41-8, Methsuximide 77-67-8, Ethosuximide 86-34-0, Phensuximide 86-35-1, Ethotoin 99-66-1 115-38-8, Mephobarbital 115-67-3, Paramethadione 125-33-7, Primidone 125-84-8, Aminoglutethimide 127-48-0, Trimethadione 298-46-4, Carbamazepine 439-14-5, Diazepam 501-68-8 1622-61-3, Clonazepam 2078-54-8, Propofol 7772-37-4, Phethenylate 22316-47-8, Clobazam 23887-31-2, Clorazepate 25451-15-4, Felbamate 28721-07-5, Oxcarbazepine 59467-70-8, Midazolam 60142-96-3, Gabapentin 68291-97-4, Zonisamide 68506-86-5, Vigabatrin 84057-84-1, Lamotrigine 93390-81-9, Fosphenytoin 97240-79-4, Topiramate 102767-28-2, Levetiracetam 103628-46-2, Sumatriptan 115103-54-3, Tiagabine 132014-88-1 157971-06-7, GYK152466
(in combination with ion-dependent cotransporter antagonist; Methods and compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)

IT 7440-09-7, Potassium, biological studies 7440-23-5, Sodium, biological studies 16887-00-6, Chloride, biological studies
(sodium potassium chloride cotransporter antagonist; Methods and ion-dependent cotransporter antagonist compds. for treating central and peripheral nervous system disorders and methods for screening the compds.)

RN 50-06-6
RN 54-31-9
RN 50-11-3
RN 50-12-4
RN 57-41-0
RN 63-98-9
RN 67-52-7D
RN 76-74-4
RN 76-75-5
RN 77-41-8
RN 77-67-8
RN 86-34-0
RN 86-35-1
RN 99-66-1
RN 115-38-8
RN 115-67-3
RN 125-33-7
RN 125-84-8
RN 127-48-0
RN 298-46-4
RN 439-14-5
RN 501-68-8
RN 1622-61-3
RN 2078-54-8
RN 7772-37-4
RN 22316-47-8
RN 23887-31-2
RN 25451-15-4
RN 28721-07-5
RN 59467-70-8
RN 60142-96-3
RN 68291-97-4

RN 68506-86-5
RN 84057-84-1
RN 93390-81-9
RN 97240-79-4
RN 102767-28-2
RN 103628-46-2
RN 115103-54-3
RN 132014-88-1
RN 157971-06-7
RN 7440-09-7
RN 7440-23-5
RN 16887-00-6

L9 ANSWER 21 OF 26 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:196849 BIOSIS
DOCUMENT NUMBER: PREV200000196849
TITLE: Sodium pump activity, not glial spatial buffering, clears potassium after epileptiform activity induced in the dentate gyrus.
AUTHOR(S): Xiong, Zhi-Qi; Stringer, Janet L. (1)
CORPORATE SOURCE: (1) Dept. of Pharmacology, Baylor College of Medicine, One Baylor Plaza, Houston, TX, 77030 USA
SOURCE: Journal of Neurophysiology (Bethesda), (Marcj, 2000) Vol. 83, No. 3, pp. 1443-1451.
ISSN: 0022-3077.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A number of mechanisms have been proposed to play a role in the regulation of activity-dependent variations in extracellular potassium concentration ((K+)o). We tested possible regulatory mechanisms for (K+)o during spontaneous recurrent epileptiform activity induced in the dentate gyrus of hippocampal slices from adult rats by perfusion with 8 mM potassium and 0-added calcium medium in an interface chamber. Local application of tetrodotoxin blocked local (K+)o changes, suggesting that potassium is réleased and taken up locally. Perfusion with barium or cesium, **blockers** of the inward rectifying potassium channel, did not alter the baseline (K+)o, the ceiling level of (K+)o reached during the burst, or the rate of (K+)o recovery after termination of the bursts. Decreasing gap junctional conductance did not change the baseline (K+)o or the half-time of recovery of the (K+)o after the bursts but did cause a decrease in the ceiling level of (K+)o. Perfusion with furosemide, which will block cation/chloride **cotransporters**, or perfusion with low chloride did not change the baseline (K+)o or the half-time of recovery of the (K+)o after the bursts but did increase the ceiling level of (K+)o. Bath or local application of ouabain, a Na+/K+-ATPase **inhibitor**, increased the baseline (K+)o, slowed the rate of (K+)o recovery, and induced spreading **depression**. These findings suggest that potassium redistribution by glia only plays a minor role in the regulation of (K+)o in this model. The major regulator of (K+)o in this model appears to be uptake via a Na+/K+-ATPase, most likely neuronal.

9 ANSWER 14 OF 26 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:89782 BIOSIS
DOCUMENT NUMBER: PREV199800089782
TITLE: Interaction between Na+/phosphate-cotransporter and the adrenoceptors in myocardial **depression**.
AUTHOR(S): Onwochei, Michael O. (1); Ofori, Abena O.; Agodoa, Irene L.
CORPORATE SOURCE: (1) Dep. Pharmacol. and Therapeutics, Med. Coll. Ohio, 3000 Arlington Ave., P.O. Box 10008, Toledo, OH 43699-0008 USA
SOURCE: Journal of Cardiovascular Pharmacology, (Jan., 1998) Vol. 31, No. 1, pp. 10-17.
ISSN: 0160-2446.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The primary objective of this study was to test the hypothesis that an increase in the alpha1-adrenoceptor tone would potentiate the myocardial biphasic contractile response to inorganic phosphate (Pi, the substrate of Na/Pi-**cotransporter** (NP)). A second aim was to determine whether activation of alpha1-adrenoceptor is necessary for the NP-mediated increase in myocardial contractility (+dP/dt). Earlier study from this laboratory showed that high concentration of Pi (10 mM) produces a biphasic contractile response: initial increase in +dP/dt was followed by decline. In another study, Pi (3.5 mM) potentiated phenylephrine (PHE)-induced increase in +dP/dt. The alpha1-adrenoceptor was not blocked in these studies, and it can still be activated by the electrical stimulation of the sympathetic nerve terminals to the heart. Additionally, alpha1-adrenoceptor-activated increases in the activity of NP have been reported in numerous studies in noncardiac tissues and cell lines; therefore it is not clear whether Pi-induced increase in +dP/dt occurs only in the presence of alpha1-adrenoceptor activation. This study was performed by using isolated perfused rat heart in the condition of controlled extracellular calcium activity (0.72 mM); fixed preload (15 mm Hg); and constant heart rate (280 beats/min) and coronary flow (8 ml/min). The electronically differentiated value of the left ventricular pressure (LVP) signal was used as an index of myocardial contractility. The data show that activation of the alpha1-adrenoceptor is not necessary for the Pi-induced increase in +dP/dt (i.e., NP-mediated increase in +dP/dt has both the alpha1-adrenoceptor-dependent and alpha1-adrenoceptor-independent components. The interaction between alpha1-adrenoceptor agonist (PHE) and Pi (10 mM) did not produce a biphasic myocardial contractile response in the presence of propranolol. Because our earlier data on myocardial biphasic contractile response to 10 mM Pi was obtained when neither the beta- nor the alpha-adrenoceptor was blocked, we carried out more studies to see whether beta-adrenoceptor plays a role in this Pi-induced biphasic response. When both the alpha- and beta-adrenoceptors were activated with norepinephrine (NE), myocardial **depression** by high Pi concentration was markedly potentiated. This myocardial **depression** did not occur in the presence of phosphonoformate, a selective **inhibitor** of NP. It also did not occur when alpha1-adrenoceptor was blocked. Our data suggest that alpha1- and beta-adrenoceptors do not interact with the cardiac NP to potentiate the Pi-induced biphasic contractile response, but they interact in a manner that potentiates Pi-induced myocardial **depression**.

L9 ANSWER 10 OF 26 USPATFULL on STN

ACCESSION NUMBER: 2003:100059 USPATFULL

TITLE: Co-administration of melanocortin receptor agonist and phosphodiesterase inhibitor for treatment of cyclic-AMP associated disorders

INVENTOR(S): Macor, John E., Guilford, CT, UNITED STATES
Carlson, Kenneth E., West Windsor, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003069169	A1	20030410
APPLICATION INFO.:	US 2002-90258	A1	20020304 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-273206P	20010302 (60)
	US 2001-273291P	20010302 (60)
	US 2001-289719P	20010509 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 2497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Co-administration of a melanocortin receptor agonist, particularly an MC-1R or MC-4R agonist, and a cAMP phosphodiesterase inhibitor is described for modulating levels of cyclic adenoise 3',5' monophosphate (cAMP) in a mammal. The inventive co-administration is useful in the treatment of diseases affected by activity of cAMP-PDE, including without limitation, inflammatory bowel disease, irritable bowel syndrome, rheumatoid arthritis, osteoarthritis, pancreatis, psoriasis, **migraine**, Alzheimer's Disease, Parkinson's disease, transplant rejection, asthma, acute respiratory distress syndrome, chronic obstructive pulmonary disease, stroke, and neurodegeneration of, and consequences of traumatic brain injury.

L9 ANSWER 9 OF 26 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2001010115 EMBASE
TITLE: The effect of sertraline on routine blood chemistry values.
AUTHOR: Catalano M.C.; Catalano G.; Kanfer S.N.; Toner L.C.; Stock S.L.; Taylor W.D.
CORPORATE SOURCE: G. Catalano, South Florida Psychiat. Center Univ., 3515 East Fletcher Ave., Tampa, FL 33613, United States
SOURCE: Clinical Neuropharmacology, (2000) 23/5 (267-270).
Refs: 26
ISSN: 0362-5664 CODEN: CLNEDB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Sertraline is an antidepressant of the selective serotonin reuptake **inhibitor** (SSRI) class. Although SSRIs are believed to have a milder side effect profile than the tricyclic antidepressants, there are some potentially serious side effects. These include hyponatremia, which has been seen with each of the SSRIs. We reviewed the charts of 246 patients treated with sertraline at a veterans' hospital. We obtained values for each patient's basic chemistry panel (**sodium**, **potassium**, **chloride**, glucose, carbon dioxide, blood urea nitrogen, and creatinine) before and after institution of sertraline therapy. We studied the patients' ages and sertraline doses to see if there was a relationship between any laboratory value changes and these variables. We found no relationship between maximum sertraline dose, age, and changes in routine blood chemistry results with the exception of a small (0.5%) contribution of maximum sertraline dose to variance in serum creatinine levels. Sertraline therapy was not noted to cause any significant changes in serum sodium levels.

L9 ANSWER 6 OF 26 USPATFULL on STN

ACCESSION NUMBER:	2002:122675 USPATFULL
TITLE:	Benzamide ligands for the thyroid receptor
INVENTOR(S):	Ryono, Denis E., Princeton, NJ, United States
PATENT ASSIGNEE(S):	Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6395784	B1	20020528	
APPLICATION INFO.:	US 2001-871347		20010531	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-210102P	20000607	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Killos, Paul J.
LEGAL REPRESENTATIVE:	Kilcoyne, John M.
NUMBER OF CLAIMS:	29
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT:	982

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB New thyroid receptor ligands are provided which have the general formula ##STR1##

in which:

X is --O--, --S--, --CH.sub.2--, --CO--, or --NH--;

R.sub.1 is halogen, trifluoromethyl, or alkyl of 1 to 6 carbons or cycloalkyl of 3 to 7 carbons;

R.sub.2 and R.sub.3 are the same or different and are hydrogen, halogen, alkyl of 1 to 4 carbons or cycloalkyl of 3 to 6 carbons, at least one of R.sub.2 and R.sub.3 being other than hydrogen;

R.sub.4 is methyl, ethyl, n-propyl or trifluoromethyl;

R.sub.5 is hydrogen or lower alkyl;

R.sub.6 is carboxylic acid, or esters or prodrugs;

R.sub.7 is hydrogen or an alkanoyl or an aroyl.

In addition, a method is provided for preventing, inhibiting or treating a disease associated with metabolism dysfunction or which is dependent upon the expression of a T.sub.3 regulated gene, wherein a compound as described above is administered in a therapeutically effective amount. Examples of such diseases associated with metabolism dysfunction or are dependent upon the expression of a T.sub.3 regulated gene include obesity, hypercholesterolemia, atherosclerosis, cardiac arrhythmias, **depression**, osteoporosis, hypothyroidism, goiter, thyroid cancer as well as glaucoma, congestive heart failure and skin disorders.

L9 ANSWER 4 OF 26 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:71074 BIOSIS
DOCUMENT NUMBER: PREV200300071074
TITLE: Methods and compositions for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms.
AUTHOR(S): Hochman, Daryl W.
ASSIGNEE: Cytoscan Sciences LLC, Seattle, WA, USA
PATENT INFORMATION: US 6495601 December 17, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 17 2002) Vol. 1265, No. 3, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The present invention relates to methods and compositions for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms. More specifically, one aspect of the present invention relates to methods and materials for treating seizure and seizure disorders, epilepsy, status epilepticus, **migraine**, spreading **depression**, intracranial hypertension; for treating the pathophysiological effects of head trauma, stroke, ischemia and hypoxia; for treating or protecting from the pathophysiological effects of neurotoxic agents such as ethanol; and for treating neurophsyciatric disorders and central nervous system edema by administering agents that modulate ionic concentrations and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride **cotransporter antagonists**. Ion-dependent cotransport **antagonists** and combinations of such compositions with other agents for treating various conditions are disclosed. The present invention also relates to methods and compositions for treating pain by administering ion-dependent **cotransporter antagonists**. Methods and compositions for enhancing cortical function, for example, in centers of cognition, learning and memory, by administering ion-dependent **cotransporter** agonists are disclosed. Methods and systems for screening drug candidate compounds for desired activities using in vitro and in vivo systems are disclosed.

L9 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:441913 CAPLUS
DOCUMENT NUMBER: 133:68975
TITLE: Methods and ion-dependent **cotransporter antagonist** compounds for treating central and peripheral nervous system disorders and methods for screening the compounds
INVENTOR(S): Hochman, Daryl
PATENT ASSIGNEE(S): Cytoscan Sciences L.L.C., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037616	A1	20000629	WO 1999-US30806	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356460	AA	20000629	CA 1999-2356460	19991222
EP 1141251	A1	20011010	EP 1999-967584	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533353	T2	20021008	JP 2000-589672	19991222

PRIORITY APPLN. INFO.: US 1998-113620P P 19981223
US 1999-326244 A 19990604
WO 1999-US30806 W 19991222

AB Methods and compns. for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms are described. Examples of the selected conditions are seizure, epilepsy, status epilepticus, **migraine**, spreading **depression**, intracranial hypertension; pathophysiol. effects of head trauma, stroke, ischemia and hypoxia; pathophysiol. effects of neurotoxic agents such as ethanol; neuropsychiatric disorders, and central nervous system edema. Treatment comprises administering agents that modulate ionic concns. and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride **cotransporter antagonists**. Electrolyte cotransport antagonists (e.g., furosemide) and combinations of such compns. with other agents are disclosed . Methods and systems for screening drug candidate compds. for desired activities using in vitro and in vivo systems are also described.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:488246 CAPLUS
DOCUMENT NUMBER: 137:57576
TITLE: Methods and compositions using ion-dependent cotransporter modulators for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms
INVENTOR(S): Hochman, Daryl W.
PATENT ASSIGNEE(S): Cytoscan Sciences L.L.C., USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S.

Ser. No. 470,637.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002082252	A1	20020627	US 2002-56528	20020123
US 6495601	B1	20021217	US 1999-470637	19991222

PRIORITY APPLN. INFO.:
US 1998-113620P P 19981223
US 1999-470637 A2 19991222
US 2001-263830P P 20010123

AB The invention discloses methods and compns. for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms. More specifically, one aspect of the invention provides methods and materials for treating seizure and seizure disorders, epilepsy, status epilepticus, **migraine**, spreading **depression**, intracranial hypertension; for treating the pathophysiol. effects of head trauma, stroke, ischemia and hypoxia; for treating or protecting from the pathophysiol. effects of neurotoxic agents such as ethanol; and for treating neurophsyciatric disorders and central nervous system edema by administering agents that modulate ionic concns. and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride **cotransporter antagonists**. Electrolyte cotransport antagonists and combinations of such compns. with other agents for treating various conditions are disclosed. The invention also discloses methods and compns. for treating pain by administering ion-dependent **cotransporter antagonists**. Methods and compns. for enhancing cortical function, e.g. in centers of cognition, learning, and memory, by administering ion-dependent cotransporter agonists are disclosed.

L9 ANSWER 3 OF 26 USPATFULL on STN